

## SEQUENCE LISTING

&lt;110&gt; Unilever plc

Unilever NV

&lt;120&gt; Production of Antibodies

&lt;130&gt; T7060

&lt;160&gt; 67

&lt;170&gt; PatentIn version 3.0

&lt;210&gt; 1

&lt;211&gt; 440

&lt;212&gt; DNA

&lt;213&gt; Artificial

&lt;220&gt;

&lt;223&gt; VHH with peptide linker

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (1)..(417)

&lt;400&gt; 1

cag	gtg	cag	ctg	cag	gag	tca	ggg	gga	gga	ttg	gtg	cag	gct	ggg	ggc	48
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1				5					10					15		
tct	ctg	aga	ctc	tcc	tgt	gca	gcc	tcg	gga	cgc	gcc	acc	agt	ggg	cat	96
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Arg	Ala	Thr	Ser	Gly	His	
			20					25					30			
ggt	cac	tat	ggt	atg	ggc	tgg	ttc	cgc	cag	gtt	cca	ggg	aag	gag	cgt	144
Gly	His	Tyr	Gly	Met	Gly	Trp	Phe	Arg	Gln	Val	Pro	Gly	Lys	Glu	Arg	
		35					40					45				
gag	ttt	gtc	gca	gct	att	agg	tgg	agt	ggt	aaa	gag	aca	tgg	tat	aaa	192
Glu	Phe	Val	Ala	Ala	Ile	Arg	Trp	Ser	Gly	Lys	Glu	Thr	Trp	Tyr	Lys	
	50					55				60						
gac	tcc	gtg	aag	ggc	cga	ttc	acc	atc	tcc	aga	gat	aac	gcc	aag	act	240
Asp	Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Thr	
65					70					75					80	

0037476-12800

acg gtt tat ctg caa atg aac agc ctg aaa cct gaa gat acg gcc gtt 288  
 Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val  
 85 90 95

tat tat tgt gcc gct cga ccg gtc cgc gtg gat gat att tcc ctg ccg 336  
 Tyr Tyr Cys Ala Ala Arg Pro Val Arg Val Asp Asp Ile Ser Leu Pro  
 100 105 110

gtt ggg ttt gac tac tgg ggc cag ggg acc cag gtc acc gtc tcc tca 384  
 Val Gly Phe Asp Tyr Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser  
 115 120 125

gaa caa aaa ctc atc tca gaa gag gat ctg aat taataagggc taagctcgaa 437  
 Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asn  
 130 135

ttc 440

<210> 2

<211> 139

<212> PRT

<213> Artificial

<400> 2

Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala Gly Gly  
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Ala Thr Ser Gly His  
 20 25 30

Gly His Tyr Gly Met Gly Trp Phe Arg Gln Val Pro Gly Lys Glu Arg  
 35 40 45

Glu Phe Val Ala Ala Ile Arg Trp Ser Gly Lys Glu Thr Trp Tyr Lys  
 50 55 60

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr  
 65 70 75 80

Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val  
 85 90 95

Tyr Tyr Cys Ala Ala Arg Pro Val Arg Val Asp Asp Ile Ser Leu Pro  
 100 105 110

Val Gly Phe Asp Tyr Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser  
 115 120 125

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asn  
 130 135

008121" 9242260

<210> 3  
 <211> 11  
 <212> PRT  
 <213> Artificial

<220>  
 <223> myc linker  
 <400> 3

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asn  
 1 5 10

<210> 4  
 <211> 471  
 <212> DNA  
 <213> Artificial

<220>  
 <223> VHH with linker  
 <220>  
 <221> CDS  
 <222> (1)..(459)

<400> 4  
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 Gln Val Gln Leu Gln Gln Ser Gly Gly Gly Leu Val Gln Ala Gly Gly  
 1 5 10 15  
 tct ctg aga ctc tcc tgt gta gct tct gaa agc agc ttc agc aac aat 96  
 Ser Leu Arg Leu Ser Cys Val Ala Ser Glu Ser Ser Phe Ser Asn Asn  
 20 25 30  
 cac atg ggc tgg tac cgc cgg gct cca ggg aac cag cgc gag ctg gtc 144  
 His Met Gly Trp Tyr Arg Arg Ala Pro Gly Asn Gln Arg Glu Leu Val  
 35 40 45  
 gca act att agt cct ggt ggt agc aca cac tat gta gac tcc gtg aag 192  
 Ala Thr Ile Ser Pro Gly Gly Ser Thr His Tyr Val Asp Ser Val Lys  
 50 55 60  
 ggc cga ttc acc atc tcc cga gac aac gcc aag aac aca gtg tat cta 240  
 Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu  
 65 70 75 80  
 caa atg gac agc ctg aaa cca gag gac acg gcc gtc tat tac tgt gct 288  
 Gln Met Asp Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys Ala  
 85 90 95  
 gcc aag ggg agg ggg ctg cag gct atg cag tac tgg ggc cag ggg acc 336  
 Ala Lys Gly Arg Gly Leu Gln Ala Met Gln Tyr Trp Gly Gln Gly Thr

008127"92426250

100										105					110					
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Leu	Val	Thr	Val	Ser	Ser	Ala	His	His	Ser	Glu	Asp	Pro	Ser	Ser	Ala					
		115						120					125							
gcc	gcc	cat	cac	cat	cac	cat	cac	ggg	gcc	gca	gaa	caa	aaa	ctc	atc	432				
Ala	Ala	His	His	His	His	His	His	Gly	Ala	Ala	Glu	Gln	Lys	Leu	Ile					
		130					135				140									
tca	gaa	gag	gat	ctg	aat	ggg	gcc	gca	tagtaacaat	tg						471				
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			20					25					30							
His	Met	Gly	Trp	Tyr	Arg	Arg	Ala	Pro	Gly	Asn	Gln	Arg	Glu	Leu	Val					
		35					40					45								
Ala	Thr	Ile	Ser	Pro	Gly	Gly	Ser	Thr	His	Tyr	Val	Asp	Ser	Val	Lys					
		50				55					60									
Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Thr	Val	Tyr	Leu					
65					70					75					80					
Gln	Met	Asp	Ser	Leu	Lys	Pro	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala					
				85					90					95						
Ala	Lys	Gly	Arg	Gly	Leu	Gln	Ala	Met	Gln	Tyr	Trp	Gly	Gln	Gly	Thr					
			100					105					110							
Leu	Val	Thr	Val	Ser	Ser	Ala	His	His	Ser	Glu	Asp	Pro	Ser	Ser	Ala					
			115					120					125							
Ala	Ala	His	His	His	His	His	His	Gly	Ala	Ala	Glu	Gln	Lys	Leu	Ile					
		130					135				140									
Ser	Glu	Glu	Asp	Leu	Asn	Gly	Ala	Ala												
		145				150														

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 <212> DNA  
 <213> Artificial

<220>

<223> VHH with linker

<220>

<221> CDS

<222> (1)..(456)

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 1 5 10 15  
 tct ctg aga ctc tcc tgt gta gcc tct gga aac acc ttc agt atc ata 96  
 Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Asn Thr Phe Ser Ile Ile  
 20 25 30  
 gct atg gcc tgg tac cgc cag gct cca ggg aag cag cgc gag gtg gtc 144  
 Ala Met Ala Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Val Val  
 35 40 45  
 gca agt att aat agt att ggc agc aca aat tat gca gac tcc gtg aag 192  
 Ala Ser Ile Asn Ser Ile Gly Ser Thr Asn Tyr Ala Asp Ser Val Lys  
 50 55 60  
 ggg cga ttc acc atc tcc aga gac aac gcc aag aac aca gtg tat ctg 240  
 Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu  
 65 70 75 80  
 caa atg agc agc ctg aaa cct gag gac acg gcc gtc tat tac tgt gct 288  
 Gln Met Ser Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys Ala  
 85 90 95  
 gcc ggt aat ttg ctg gtt aag agg cct tac tgg ggc cag ggg acc ctg 336  
 Ala Gly Asn Leu Leu Val Lys Arg Pro Tyr Trp Gly Gln Gly Thr Leu  
 100 105 110  
 gtc acc gtc tcc tca gaa ccc aag aca cca aaa cca caa cca gcg gcc 384  
 Val Thr Val Ser Ser Glu Pro Lys Thr Pro Lys Pro Gln Pro Ala Ala  
 115 120 125  
 gcc cat cac cat cac cat cac ggg gcc gca gaa caa aaa ctc atc tca 432  
 Ala His His His His His His Gly Ala Ala Glu Gln Lys Leu Ile Ser  
 130 135 140  
 gaa gag gat ctg aat ggg gcc gca tagtaacaat tg 468  
 Glu Glu Asp Leu Asn Gly Ala Ala  
 145 150

<210> 7

<211> 152

00346 944660

<222> (1) . . (450)

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 1 5 10 15  
  
 gct ggg ggc cct ctg agg ctc tcc tgt gca gcc tct gga cgc acc ttc 96  
 Ala Gly Gly Pro Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe  
 20 25 30  
  
 agt aac tat gcc gtg ggc tgg ttc cgc cag gct cca ggg aag gag cgt 144  
 Ser Asn Tyr Ala Val Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg  
 35 40 45  
  
 gag ttt gtc gct gct att agc cgt gat ggt ggg cgc aca tac tat gcg 192  
 Glu Phe Val Ala Ala Ile Ser Arg Asp Gly Gly Arg Thr Tyr Tyr Ala  
 50 55 60  
  
 gac tcc gtg aag ggc cga ttc gcc gtc tcc aga gac tac gcc gag aac 240  
 Asp Ser Val Lys Gly Arg Phe Ala Val Ser Arg Asp Tyr Ala Glu Asn  
 65 70 75 80  
  
 acg gtg tat ctg caa atg aac agc ctg aaa cct gag gac acg gcc gtt 288  
 Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val  
 85 90 95  
  
 tat tac tgt aac aca agg gcc tac tgg ggc cag ggg acc cag gtc acc 336  
 Tyr Tyr Cys Asn Thr Arg Ala Tyr Trp Gly Gln Gly Thr Gln Val Thr  
 100 105 110  
  
 gtc tcc tca gcg cac cac agc gaa gac ccc agc tcc gcg gcc gcc cat 384  
 Val Ser Ser Ala His His Ser Glu Asp Pro Ser Ser Ala Ala Ala His  
 115 120 125  
  
 cac cat cac cat cac ggg gcc gca gaa caa aaa ctc atc tca gaa gag 432  
 His His His His His Gly Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu  
 130 135 140  
  
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 Asp Leu Asn Gly Ala Ala  
 145 150

<210> 9

<211> 150

<212> PRT

<213> Artificial

<400> 9

Thr Met Ala Gln Val Lys Leu Gln Gln Ser Gly Gly Gly Leu Val Gln  
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 Ala Gly Gly Pro Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe  
 20 25 30  
  
 Ser Asn Tyr Ala Val Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg  
 35 40 45

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Glu Phe Val Ala Ala Ile Ser Arg Asp Gly Gly Arg Thr Tyr Tyr Ala  
50 55 60

Asp Ser Val Lys Gly Arg Phe Ala Val Ser Arg Asp Tyr Ala Glu Asn  
65 70 75 80

Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val  
85 90 95

Tyr Tyr Cys Asn Thr Arg Ala Tyr Trp Gly Gln Gly Thr Gln Val Thr  
100 105 110

Val Ser Ser Ala His His Ser Glu Asp Pro Ser Ser Ala Ala Ala His  
115 120 125

His His His His His Gly Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu  
130 135 140

Asp Leu Asn Gly Ala Ala  
145 150

<210> 10

<211> 471

<212> DNA

<213> Artificial

<220>

<223> VHH with linker

<220>

<221> CDS

<222> (1)..(459)

<400> 10

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1 5 10 15

gct ggg ggc cct ctg agg ctc tcc tgt gca gcc tct gga cgc acc ttc 96  
Ala Gly Gly Pro Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe  
20 25 30

agt aac tat gcc gtg ggc tgg ttc cgc cag gct cca ggg aag gag cgt 144  
Ser Asn Tyr Ala Val Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg  
35 40 45

gag ttt gtc gct gct att agc cgt gat ggt ggg cgc aca tac tat gcg 192  
Glu Phe Val Ala Ala Ile Ser Arg Asp Gly Gly Arg Thr Tyr Tyr Ala  
50 55 60

gac tcc gtg aag ggc cga ttc gcc gtc tcc aga gac tac gcc gag aac 240

0087227 92426260



Asp 65	Ser	Val	Lys	Gly	Arg 70	Phe	Ala	Val	Ser	Arg 75	Asp	Tyr	Ala	Glu	Asn 80								
acg	gtg	tat	ctg	caa	atg	aac	agc	ctg	aaa	cct	gag	gac	acg	gcc	gtt	288							
Thr	Val	Tyr	Leu	Gln 85	Met	Asn	Ser	Leu	Lys 90	Pro	Glu	Asp	Thr	Ala 95	Val								
tat	tac	tgt	aac	aca	agg	gcc	tac	tgg	ggc	cag	ggg	acc	cag	gtc	acc	336							
Tyr	Tyr	Cys	Asn 100	Thr	Arg	Ala	Tyr	Trp 105	Gly	Gln	Gly	Thr	Gln 110	Val	Thr								
gtc	tcc	tca	gcg	cac	cac	agc	gaa	gac	ccc	agc	tcc	gcg	gcc	gcc	cat	384							
Val	Ser	Ser 115	Ala	His	His	Ser	Glu 120	Asp	Pro	Ser	Ser	Ala 125	Ala	Ala	His								
cac	cat	cac	cat	cac	ggg	gcc	gca	gaa	caa	aaa	ctc	atc	tca	gaa	gag	432							
His	His	His	His	His	Gly 130	Ala 135	Ala	Glu	Gln	Lys	Leu 140	Ile	Ser	Glu	Glu								
gat	ctg	aat	agt	gag	aaa	gat	gag	cta	tgataacaat tg							471							
Asp 145	Leu	Asn	Ser	Glu	Lys 150	Asp	Glu	Leu															
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Ala	Gly	Gly	Pro 20	Leu	Arg	Leu	Ser	Cys 25	Ala	Ala	Ser	Gly	Arg 30	Thr	Phe								
Ser	Asn	Tyr 35	Ala	Val	Gly	Trp 40	Phe	Arg	Gln	Ala	Pro	Gly 45	Lys	Glu	Arg								
Glu	Phe 50	Val	Ala	Ala	Ile	Ser 55	Arg	Asp	Gly	Gly	Arg 60	Thr	Tyr	Tyr	Ala								
Asp 65	Ser	Val	Lys	Gly	Arg 70	Phe	Ala	Val	Ser	Arg 75	Asp	Tyr	Ala	Glu	Asn 80								
Thr	Val	Tyr	Leu	Gln 85	Met	Asn	Ser	Leu	Lys 90	Pro	Glu	Asp	Thr	Ala 95	Val								
Tyr	Tyr	Cys	Asn 100	Thr	Arg	Ala	Tyr	Trp 105	Gly	Gln	Gly	Thr	Gln 110	Val	Thr								
Val	Ser	Ser 115	Ala	His	His	Ser	Glu 120	Asp	Pro	Ser	Ser	Ala 125	Ala	Ala	His								

His His His His His Gly Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu  
 130 135 140

Asp Leu Asn Ser Glu Lys Asp Glu Leu  
 145 150

<210> 12

<211> 38

<212> DNA

<213> Artificial

<220>

<223> synthetic insert

<400> 12  
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38

<210> 13

<211> 42

<212> DNA

<213> Artificial

<220>

<223> synthetic insert

<400> 13  
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42

<210> 14

<211> 31

<212> DNA

<213> Artificial

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<223> synthetic insert

<400> 14  
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31

<210> 15

<211> 23

<212> DNA

008F2F "9244260

<213> Artificial

<220>

<223> synthetic insert

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<210> 16

<211> 22

<212> DNA

<213> Artificial

<220>

<223> primer

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22

<210> 17

<211> 39

<212> DNA

<213> Artificial

<220>

<223> primer

<400> 17

gaattcccat ggtttacact cgaggtcctc tccaaatga

39

<210> 18

<211> 189

<212> DNA

<213> Artificial

<220>

<223> PCR product

<400> 18

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60

ggattgatgt gatattcca ctgacgtaag ggatgacgca caatcccact atccttcgca

120

agacccttcc tttatataag gaagttcatt tcatttggag aggacctga gtgtaaacca

180

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tggaattc

189

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21

<210> 20

<211> 40

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40

<210> 21

<211> 35

<212> DNA

<213> Artificial

<220>

<223> synthetic insert

<400> 21

ttcttcttgt ctctacactt ctcttattcc tagta

35

<210> 22

<211> 35

<212> DNA

<213> Artificial

003213024250



Thr Leu Leu Leu Phe Leu Val Ile Ser His Ser Cys Arg Ala Gln Val  
20 25 30

Gln Leu

&lt;210&gt; 29

&lt;211&gt; 21

&lt;212&gt; DNA

&lt;213&gt; Artificial

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 29

gacatcccat ggcaagcatc a

21

&lt;210&gt; 30

&lt;211&gt; 21

&lt;212&gt; DNA

&lt;213&gt; Artificial

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 30

aagcttggtta acagccctta a

21

&lt;210&gt; 31

&lt;211&gt; 21

&lt;212&gt; DNA

&lt;213&gt; Artificial

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 31

agggttggtta acaaacttga t

21

&lt;210&gt; 32

&lt;211&gt; 44

&lt;212&gt; DNA

&lt;213&gt; Artificial

009727 92426260

239



cag gtg cag ctg cag  
Gln Val Gln Leu Gln  
80

254

&lt;210&gt; 35

&lt;211&gt; 84

&lt;212&gt; PRT

&lt;213&gt; Artificial

&lt;400&gt; 35

Met Ala Ser Ile Thr Ala Ser His His Phe Val Ser Arg Ser Gln Thr  
1 5 10 15

Ser Leu Asp Thr Lys Ser Thr Leu Ser Gln Ile Gly Leu Arg Asn His  
20 25 30

Thr Leu Thr His Asn Gly Leu Arg Ala Val Asn Lys Leu Asp Gly Leu  
35 40 45

Gln Ser Arg Thr Asn Thr Lys Val Thr Pro Lys Met Ala Ser Arg Thr  
50 55 60

Glu Thr Lys Arg Pro Gly Cys Ser Ala Thr Ile Val Cys Gly Lys Gln  
65 70 75 80

Val Gln Leu Gln

&lt;210&gt; 36

&lt;211&gt; 18

&lt;212&gt; DNA

&lt;213&gt; Artificial

&lt;220&gt;

&lt;223&gt; synthetic insert

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18

&lt;210&gt; 37

&lt;211&gt; 10

&lt;212&gt; DNA

&lt;213&gt; Artificial

003746-1300

&lt;220&gt;

&lt;223&gt; synthetic insert

<400> 37  
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10

&lt;210&gt; 38

&lt;211&gt; 24

&lt;212&gt; DNA

&lt;213&gt; Artificial

&lt;220&gt;

&lt;223&gt; PCR primer

<400> 38  
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24

&lt;210&gt; 39

&lt;211&gt; 60

&lt;212&gt; DNA

&lt;213&gt; Artificial

&lt;220&gt;

&lt;223&gt; PCR primer

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&lt;210&gt; 40

&lt;211&gt; 26

&lt;212&gt; PRT

&lt;213&gt; Artificial

&lt;220&gt;

&lt;223&gt; linker

&lt;400&gt; 40

Thr	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser
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Gly	Gly	Gly	Gly	Ser	Asp	Ile	Glu	Leu	Thr
			20					25	

<213> Artificial

<223> PCR primer

20

<213> Artificial

<223> PCR primer

19

<213> Artificial

<223> synthetic insert

30

<213> Artificial

<223> synthetic insert

<400> 44  
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22

<210> 45

<211> 29

<212> DNA

<213> Artificial

<220>

<223> synthetic insert

<400> 45  
gatccacctc gagtgtaaac catggcccg

29

<210> 46

<211> 29

<212> DNA

<213> Artificial

<220>

<223> synthetic insert

<400> 46  
ctagcgggcc atggtttaca ctcgaggtg

29

<210> 47

<211> 20

<212> DNA

<213> Artificial

<220>

<223> PCR primer

<400> 47  
attgcctacg gcagccgctg

20

<210> 48

<211> 51

<212> DNA

<213> Artificial

09737476 41300





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65						70					75					
aag	act	acg	gtt	tat	ctg	caa	atg	aac	agc	ctg	aaa	cct	gaa	gat	acg	287
Lys	Thr	Thr	Val	Tyr	Leu	Gln	Met	Asn	Ser	Leu	Lys	Pro	Glu	Asp	Thr	
80					85					90					95	
gcc	gtt	tat	tat	tgt	gcc	gct	cga	ccg	gtc	cgc	gtg	gat	gat	att	tcc	335
Ala	Val	Tyr	Tyr	Cys	Ala	Ala	Arg	Pro	Val	Arg	Val	Asp	Asp	Ile	Ser	
				100					105					110		
ctg	ccg	gtt	ggg	ttt	gac	tac	tgg	ggc	cag	ggg	acc	cag	gtc	acc	gtc	383
Leu	Pro	Val	Gly	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Gln	Val	Thr	Val	
			115					120					125			
tcc	tca	gaa	ccc	aag	aca	cca	aaa	cca	caa	cca	caa	cca	caa	cca	caa	431
Ser	Ser	Glu	Pro	Lys	Thr	Pro	Lys	Pro	Gln	Pro	Gln	Pro	Gln	Pro	Gln	
		130					135					140				
cca	caa	ccc	aat	cct	aca	aca	gaa	tcc	aag	tgt	ccc	aaa	tgt	cca	gcc	479
Pro	Gln	Pro	Asn	Pro	Thr	Thr	Glu	Ser	Lys	Cys	Pro	Lys	Cys	Pro	Ala	
	145					150					155					
cct	gag	ctc	ctg	gga	ggg	ccc	tca	gtc	ttc	atc	ttc	ccc	ccg	aaa	ccc	527
Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Lys	Pro	
160					165					170					175	
aag	gac	gtc	ctc	tcc	att	tct	ggg	agg	ccc	gag	gtc	acg	tgc	gtt	gtg	575
Lys	Asp	Val	Leu	Ser	Ile	Ser	Gly	Arg	Pro	Glu	Val	Thr	Cys	Val	Val	
				180					185					190		
gta	gac	gtg	ggc	cag	gaa	gac	ccc	gag	gtc	agt	ttc	aac	tgg	tac	att	623
Val	Asp	Val	Gly	Gln	Glu	Asp	Pro	Glu	Val	Ser	Phe	Asn	Trp	Tyr	Ile	
			195					200					205			
gat	ggc	gca	gag	gtg	cga	acg	gcc	aac	acg	agg	cca	aaa	gag	gaa	cag	671
Asp	Gly	Ala	Glu	Val	Arg	Thr	Ala	Asn	Thr	Arg	Pro	Lys	Glu	Glu	Gln	
		210					215					220				
ttc	aac	agc	acg	tac	cgc	gtg	gtc	agc	gtc	ctg	ccc	atc	cag	cac	cag	719
Phe	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Pro	Ile	Gln	His	Gln	
	225					230					235					
gac	tgg	ctg	acg	ggg	aaa	gag	ttc	aaa	tgc	aag	gtc	aac	aac	aaa	gct	767
Asp	Trp	Leu	Thr	Gly	Lys	Glu	Phe	Lys	Cys	Lys	Val	Asn	Asn	Lys	Ala	
240					245					250					255	
ctc	ccg	gcc	ccc	atc	gag	aag	acc	atc	tcc	aag	gcc	aaa	ggg	cag	acc	815
Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Thr	
				260					265					270		
cgg	gag	ccg	cag	gtg	tac	gcc	ctg	gcc	cca	cac	cgg	gaa	gag	ctg	gcc	863
Arg	Glu	Pro	Gln	Val	Tyr	Ala	Leu	Ala	Pro	His	Arg	Glu	Glu	Leu	Ala	
			275					280					285			
aag	gac	acc	gtg	agc	gta	acc	tgc	ctg	gtc	aaa	ggc	ttc	tac	cca	cct	911
Lys	Asp	Thr	Val	Ser	Val	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Pro	
		290					295					300				
gat	atc	aac	gtt	gag	tgg	cag	agg	aac	ggt	cag	ccg	gag	tca	gag	ggc	959
Asp	Ile	Asn	Val	Glu	Trp	Gln	Arg	Asn	Gly	Gln	Pro	Glu	Ser	Glu	Gly	
	305					310					315					
acc	tac	gcc	acc	acg	cca	ccc	cag	ctg	gac	aac	gac	ggg	acc	tac	ttc	1007
Thr	Tyr	Ala	Thr	Thr	Pro	Pro	Gln	Leu	Asp	Asn	Asp	Gly	Thr	Tyr	Phe	
320					325					330					335	

09737476 121800

Glu Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys  
165 170 175



Asp Val Leu Ser Ile Ser Gly Arg Pro Glu Val Thr Cys Val Val Val  
 180 185 190

Asp Val Gly Gln Glu Asp Pro Glu Val Ser Phe Asn Trp Tyr Ile Asp  
 195 200 205

Gly Ala Glu Val Arg Thr Ala Asn Thr Arg Pro Lys Glu Glu Gln Phe  
 210 215 220

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp  
 225 230 235 240

Trp Leu Thr Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Ala Leu  
 245 250 255

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Thr Arg  
 260 265 270

Glu Pro Gln Val Tyr Ala Leu Ala Pro His Arg Glu Glu Leu Ala Lys  
 275 280 285

Asp Thr Val Ser Val Thr Cys Leu Val Lys Gly Phe Tyr Pro Pro Asp  
 290 295 300

Ile Asn Val Glu Trp Gln Arg Asn Gly Gln Pro Glu Ser Glu Gly Thr  
 305 310 315 320

Tyr Ala Thr Thr Pro Pro Gln Leu Asp Asn Asp Gly Thr Tyr Phe Leu  
 325 330 335

Tyr Ser Lys Leu Ser Val Gly Lys Asn Thr Trp Gln Arg Gly Glu Thr  
 340 345 350

Phe Thr Cys Val Val Met His Glu Ala Leu His Asn His Tyr Thr Gln  
 355 360 365

Lys Ser Ile Thr Gln Ser Ser Gly Lys  
 370 375

<210> 56

<211> 1172

<212> DNA

<213> Artificial

<220>

<223> hinge-HCV33-CH2-CH3-SEKDEL

09232476 131800

$\langle 222 \rangle \quad (3) \dots (1154)$ 

cc atg gag gtg cag ctg cag gag tca ggg gga gga ttg gtg cag gct 47  
Met Glu Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala  
1 5 10 15

ggg ggc tct ctg aga ctc tcc tgt gca gcc tcg gga cgc gcc acc agt 95  
Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Ala Thr Ser  
20 25 30

ggt cat ggt cac tat ggt atg ggc tgg ttc cgc cag gtt cca ggg aag 143  
Gly His Gly His Tyr Gly Met Gly Trp Phe Arg Gln Val Pro Gly Lys  
35 40 45

gag cgt gag ttt gtc gca gct att agg tgg agt ggt aaa gag aca tgg 191  
Glu Arg Glu Phe Val Ala Ala Ile Arg Trp Ser Gly Lys Glu Thr Trp  
50 55 60

tat aaa gac tcc gtg aag ggc cga ttc acc atc tcc aga gat aac gcc 239  
Tyr Lys Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala  
65 70 75

aag act acg gtt tat ctg caa atg aac agc ctg aaa cct gaa gat acg 287  
Lys Thr Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr  
80 85 90 95

```
gcc gtt tat tat tgt gcc gct cga ccg gtc cgc gtg gat gat att tcc      335  
Ala Val Tyr Tyr Cys Ala Ala Arg Pro Val Arg Val Asp Asp Ile Ser  
          100                      105                  110
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ctg ccg gtt ggg ttt gac tac tgg ggc cag ggg acc cag gtc acc gtc 383  
Leu Pro Val Gly Phe Asp Tyr Trp Gly Gln Gly Thr Gln Val Thr Val  
115 120 125

tcc tca gaa ccc aag aca cca aaa cca caa cca caa cca caa cca caa 431  
Ser Ser Glu Pro Lys Thr Pro Lys Pro Gln Pro Gln Pro Gln Pro Gln  
130 135 140

cca caa ccc aat cct aca aca gaa tcc aag tgt ccc aaa tgt cca gcc 479  
Pro Gln Pro Asn Pro Thr Thr Glu Ser Lys Cys Pro Lys Cys Pro Ala  
145 150 155

cct gag ctc ctg gga ggg ccc tca gtc ttc atc ttc ccc ccg aaa ccc 527  
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro  
160 165 170 175

aag gac gtc ctc tcc att tct ggg agg ccc gag gtc acg tgc gtt gtg 575  
Lys Asp Val Leu Ser Ile Ser Gly Arg Pro Glu Val Thr Cys Val Val  
180 185 190

gta gac gtg ggc cag gaa gac ccc gag gtc agt ttc aac tgg tac att 623  
Val Asp Val Gly Gln Glu Asp Pro Glu Val Ser Phe Asn Trp Tyr Ile  
195 200 205

gat ggc gca gag gtg cga acg gcc aac acg agg cca aaa gag gaa cag 671  
Asp Gly Ala Glu Val Arg Thr Ala Asn Thr Arg Pro Lys Glu Glu Gln  
210 215 220

ttc aac agc acg tac cgc gtg gtc agc gtc ctg ccc atc cag cac cag 719  
Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln  
225 230 235

<210> 57

<211> 383

&lt;212&gt; PRT

<213> Artificial

<400> 57

Met Glu Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala Gly  
1 5 10 15

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Ala Thr Ser Gly  
20 25 30

His Gly His Tyr Gly Met Gly Trp Phe Arg Gln Val Pro Gly Lys Glu  
35 40 45

Arg Glu Phe Val Ala Ala Ile Arg Trp Ser Gly Lys Glu Thr Trp Tyr  
50 55 60

Lys 65	Asp	Ser	Val	Lys 70	Gly	Arg	Phe	Thr	Ile	Ser 75	Arg	Asp	Asn	Ala	Lys 80
Thr	Thr	Val	Tyr	Leu 85	Gln	Met	Asn	Ser	Leu 90	Lys	Pro	Glu	Asp	Thr 95	Ala
Val	Tyr	Tyr	Cys 100	Ala	Ala	Arg	Pro	Val 105	Arg	Val	Asp	Asp	Ile 110	Ser	Leu
Pro	Val	Gly 115	Phe	Asp	Tyr	Trp	Gly 120	Gln	Gly	Thr	Gln	Val 125	Thr	Val	Ser
Ser	Glu 130	Pro	Lys	Thr	Pro	Lys 135	Pro	Gln	Pro	Gln	Pro 140	Gln	Pro	Gln	Pro
Gln 145	Pro	Asn	Pro	Thr	Thr 150	Glu	Ser	Lys	Cys	Pro 155	Lys	Cys	Pro	Ala	Pro 160
Glu	Leu	Leu	Gly	Gly 165	Pro	Ser	Val	Phe	Ile 170	Phe	Pro	Pro	Lys	Pro 175	Lys
Asp	Val	Leu	Ser 180	Ile	Ser	Gly	Arg	Pro 185	Glu	Val	Thr	Cys	Val 190	Val	Val
Asp	Val	Gly 195	Gln	Glu	Asp	Pro	Glu 200	Val	Ser	Phe	Asn	Trp 205	Tyr	Ile	Asp
Gly 210	Ala	Glu	Val	Arg	Thr	Ala 215	Asn	Thr	Arg	Pro	Lys 220	Glu	Glu	Gln	Phe
Asn 225	Ser	Thr	Tyr	Arg	Val 230	Val	Ser	Val	Leu	Pro 235	Ile	Gln	His	Gln	Asp 240
Trp	Leu	Thr	Gly	Lys 245	Glu	Phe	Lys	Cys	Lys 250	Val	Asn	Asn	Lys	Ala 255	Leu
Pro	Ala	Pro	Ile 260	Glu	Lys	Thr	Ile	Ser 265	Lys	Ala	Lys	Gly	Gln 270	Thr	Arg
Glu	Pro	Gln 275	Val	Tyr	Ala	Leu	Ala 280	Pro	His	Arg	Glu	Glu 285	Leu	Ala	Lys
Asp	Thr 290	Val	Ser	Val	Thr	Cys 295	Leu	Val	Lys	Gly	Phe 300	Tyr	Pro	Pro	Asp
Ile 305	Asn	Val	Glu	Trp	Gln 310	Arg	Asn	Gly	Gln	Pro 315	Glu	Ser	Glu	Gly	Thr 320
Tyr	Ala	Thr	Thr	Pro 325	Pro	Gln	Leu	Asp	Asn 330	Asp	Gly	Thr	Tyr	Phe 335	Leu

Tyr Ser Lys Leu Ser Val Gly Lys Asn Thr Trp Gln Arg Gly Glu Thr  
340 345 350

Phe Thr Cys Val Val Met His Glu Ala Leu His Asn His Tyr Thr Gln  
355 360 365

Lys Ser Ile Thr Gln Ser Ser Gly Lys Ser Glu Lys Asp Glu Leu  
370 375 380

<210> 58

<211> 31

<212> DNA

<213> Artificial

<220>

<223> PCR primer

<400> 58

aggggacca ggtcacgctc tcttcagaac c

31

<210> 59

<211> 37

<212> DNA

<213> Artificial

<220>

<223> PCR primer

<400> 59

gagctttgtt gttgaccttg catttgaact ctttccc

37

<210> 60

<211> 26

<212> DNA

<213> Artificial

<220>

<223> PCR primer

<400> 60

caaattgcaag gtcaacaaca aagctc

26

<210> 61

<211> 42

<212> DNA

<213> Artificial

<220>

<223> PCR primer

<400> 61

ttcgagctcg aattcttatt atttaccoga agactgggtg at

42

<210> 62

<211> 27

<212> DNA

<213> Artificial

<220>

<223> sequencing primer

<400> 62

ctgaggagac ggtgacctgg gtccct

27

<210> 63

<211> 46

<212> DNA

<213> Artificial

<220>

<223> PCR primer

<400> 63

agcccctgag ctctctgggag ggccctcagt cttcatcttc ccccg

46

<210> 64

<211> 61

<212> DNA

<213> Artificial

<220>

<223> PCR primer

<400> 64

ttcgagctcg aattcttatt atttaccoga agactgggtg atggatttct ggggtgtagtg

60

008727 924260

<210> 65

<211> 79

<212> DNA

<213> Artificial

<220>

<223> PCR primer

<400> 65

ttcgagctcg aattcttatt atagctcatc tttctcagat ttacccgaag actgggtgat 60  
ggatttctgg gtgtagtgg 79

<210> 66

<211> 461

<212> DNA

<213> Artificial

<220>

<223> VHH with linker

<220>

<221> CDS

<222> (3)..(449)

<400> 66

cc atg gcc cag gtg cag ctg cag gag tct ggg gga ggc ttg gtg cag 47  
Met Ala Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln  
1 5 10 15

gct ggg ggg tct ctg agg ctc tcc tgt gca gcc tct gga agc att ttc 95  
Ala Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Ile Phe  
20 25 30

aga cgt ccg cat atg ggt tgg ttc cgc cag gct cca ggg cag gag cgc 143  
Arg Arg Pro His Met Gly Trp Phe Arg Gln Ala Pro Gly Gln Glu Arg  
35 40 45

gag ttg gtc gca ctg att tct gcg ggt ggt cgt aca tgg tat gca gac 191  
Glu Leu Val Ala Leu Ile Ser Ala Gly Gly Arg Thr Trp Tyr Ala Asp  
50 55 60

tcc gtg aag ggc cga ttc acc atc tcc aga gac aac gcc aag aac acg 239  
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr  
65 70 75

ctg tat ctg caa atg aac agc ctg aaa cct gag gac acg gcc gtt tat 287

008727 "3444660

Leu Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr  
 80 85 90 95

tac tgt act gcc ggg ggt tgc tac tgg ggc cag ggg acc cag gtc acc 335  
 Tyr Cys Thr Ala Gly Gly Ser Tyr Trp Gly Gln Gly Thr Gln Val Thr  
 100 105 110

gtc gcc tca gaa ccc aag aca cca aaa cca caa cca gcg gcc gcc cat 383  
 Val Ala Ser Glu Pro Lys Thr Pro Lys Pro Gln Pro Ala Ala Ala His  
 115 120 125

cac cat cac cat cac ggg gcc gca gaa caa aaa ctc atc tca gaa gag 431  
 His His His His His Gly Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu  
 130 135 140

gat ctg aat ggg gcc gca tagtaacaat tg 461  
 Asp Leu Asn Gly Ala Ala  
 145

<210> 67  
 <211> 149  
 <212> PRT  
 <213> Artificial

<400> 67

Met Ala Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala  
 1 5 10 15

Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Ile Phe Arg  
 20 25 30

Arg Pro His Met Gly Trp Phe Arg Gln Ala Pro Gly Gln Glu Arg Glu  
 35 40 45

Leu Val Ala Leu Ile Ser Ala Gly Gly Arg Thr Trp Tyr Ala Asp Ser  
 50 55 60

Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu  
 65 70 75 80

Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr  
 85 90 95

Cys Thr Ala Gly Gly Ser Tyr Trp Gly Gln Gly Thr Gln Val Thr Val  
 100 105 110

Ala Ser Glu Pro Lys Thr Pro Lys Pro Gln Pro Ala Ala Ala His His  
 115 120 125

His His His His Gly Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu Asp  
 130 135 140

0034216100



Leu Asn Gly Ala Ala  
145

0034134260